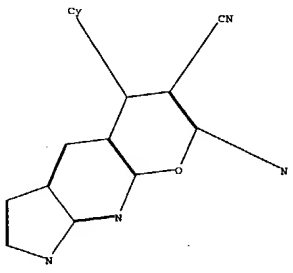
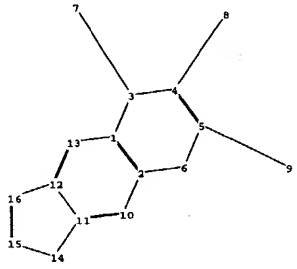
C:\stnweb\Queries\9.str





chain nodes :
7 8
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15 16
ring/chain nodes :
9
chain bonds :
3-7 4-8 5-9
ring bonds :
1-3 1-2 1-13 2-6 2-10 3-4 4-5 5-6 10-11 11-12 11-14 12-13 12-16 14-15 15-16
exact/norm bonds :
1-3 2-6 3-4 3-7 4-5 5-6 5-9 11-14 14-15
exact bonds :
4-8 12-16 15-16
normalized bonds :
1-2 1-13 2-10 10-11 11-12 12-13
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 9:CLASS 10:Atom 11:Atom
12:Atom 13:Atom 14:Atom 15:Atom 16:Atom

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 5	FEB 05	German (DE) application and patent publication number format changes
NEWS 6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 8	MAR 03	FRANCEPAT now available on STN
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NEWS 14	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
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NEWS 16	APR 27	NLDB: New search and display fields available

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:43:45 ON 30 APR 2004

=> **file reg**

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 15:43:51 ON 30 APR 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 APR 2004 HIGHEST RN 677701-51-8
DICTIONARY FILE UPDATES: 28 APR 2004 HIGHEST RN 677701-51-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

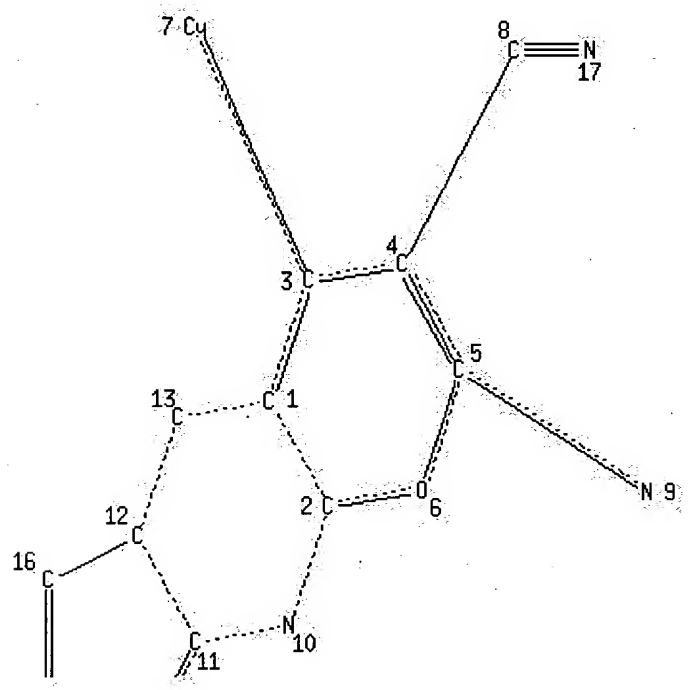
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

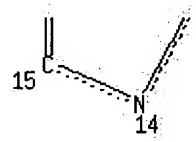
Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Page 1-A

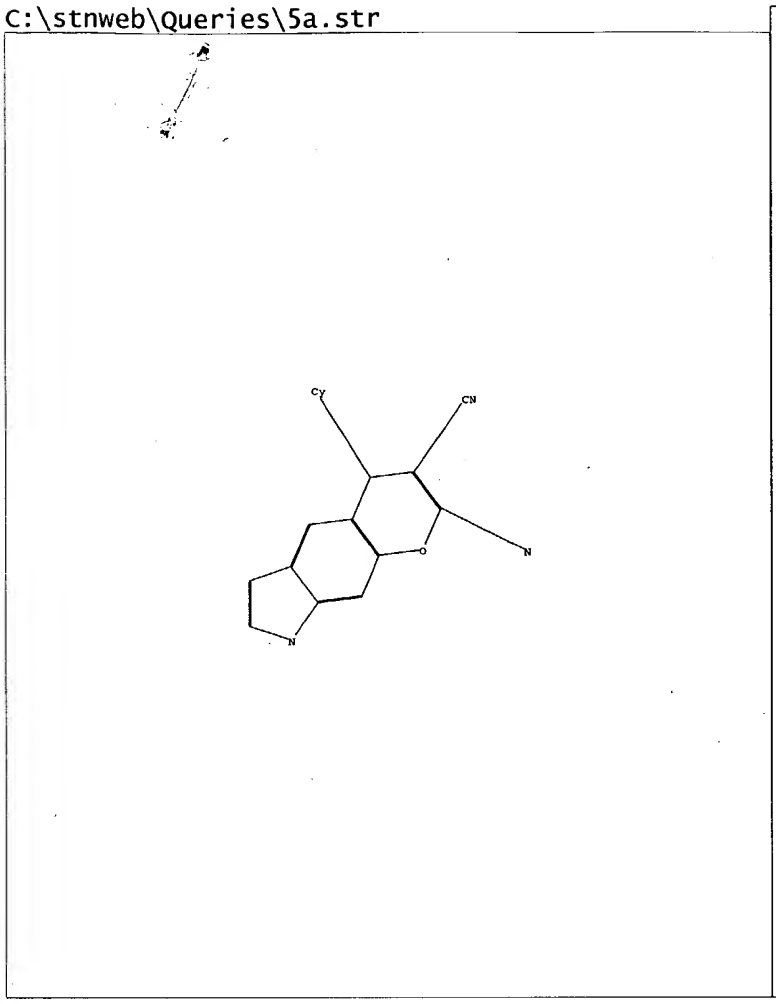


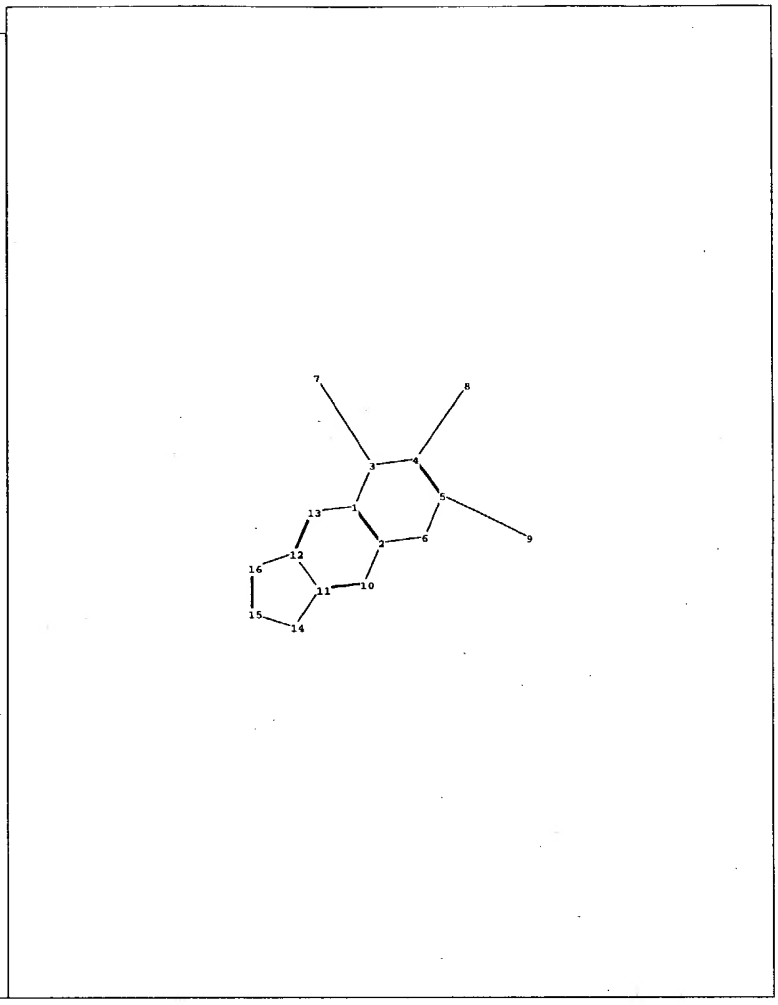
Page 2-A
NODE ATTRIBUTES:

NSPEC	IS R	AT	1
NSPEC	IS R	AT	2
NSPEC	IS R	AT	3
NSPEC	IS R	AT	4
NSPEC	IS R	AT	5
NSPEC	IS R	AT	6
NSPEC	IS C	AT	7
NSPEC	IS C	AT	8
NSPEC	IS RC	AT	9
NSPEC	IS R	AT	10

```
NSPEC   IS R      AT  11
NSPEC   IS R      AT  12
NSPEC   IS R      AT  13
NSPEC   IS R      AT  14
NSPEC   IS R      AT  15
NSPEC   IS R      AT  16
NSPEC   IS C      AT  17
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT   8  9 17
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  17

STEREO ATTRIBUTES: NONE


=> s l1
SAMPLE SEARCH INITIATED 15:44:51 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      1 TO ITERATE

100.0% PROCESSED       1 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            1 TO       80
PROJECTED ANSWERS:               0 TO        0

L2             0 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 15:44:55 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      6 TO ITERATE

100.0% PROCESSED       6 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

L3             0 SEA SSS FUL L1

=>
```

C:\stnweb\Queries\5a.str





chain nodes :
7 8
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15 16
ring/chain nodes :
9
chain bonds :
3-7 4-8 5-9
ring bonds :
1-3 1-2 1-13 2-6 2-10 3-4 4-5 5-6 10-11 11-12 11-14 12-13 12-16 14-15 15-16
exact/norm bonds :
3-7 5-9 11-14 14-15
exact bonds :
1-3 2-6 3-4 4-5 4-8 5-6 12-16 15-16
normalized bonds :
1-2 1-13 2-10 10-11 11-12 12-13
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 9:CLASS 10:Atom 11:Atom
12:Atom 13:Atom 14:Atom 15:Atom 16:Atom

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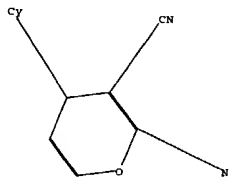

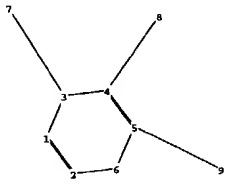

hain nodes :
7 8
ing nodes :
1 2 3 4 5 6
ing/chain nodes :
9
hain bonds :
3-7 4-8 5-9
ing bonds :
1-3 1-2 2-6 3-4 4-5 5-6
xact/norm bonds :
1-2 3-7 5-9
xact bonds :
1-3 2-6 3-4 4-5 4-8 5-6

atch level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 9:CLASS

```
* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
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 NEWS  3  JAN 27   Source of Registration (SR) information in REGISTRY updated
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               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:24:06 ON 30 APR 2004

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 15:24:11 ON 30 APR 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

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provided by InfoChem.

STRUCTURE FILE UPDATES:   28 APR 2004  HIGHEST RN 677701-51-8
DICTIONARY FILE UPDATES:  28 APR 2004  HIGHEST RN 677701-51-8
```

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

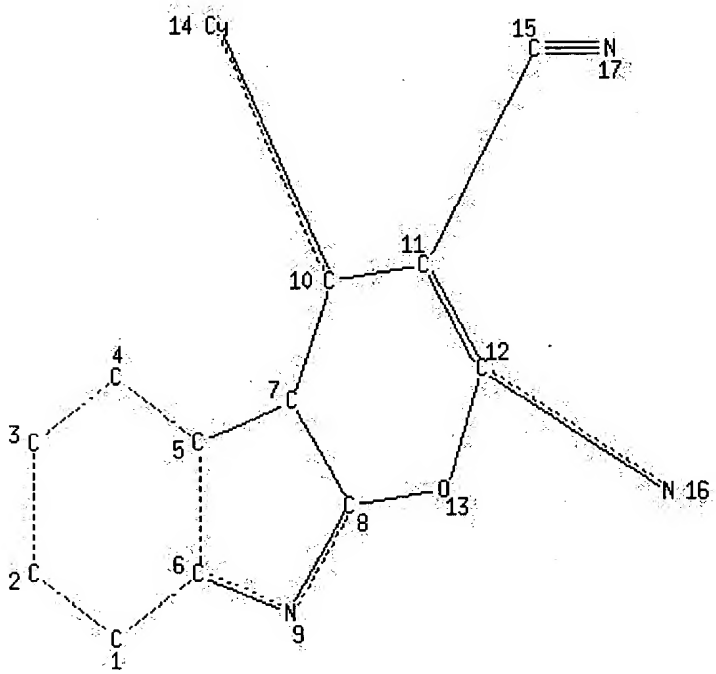
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L1 STRUCTURE UPLOADED

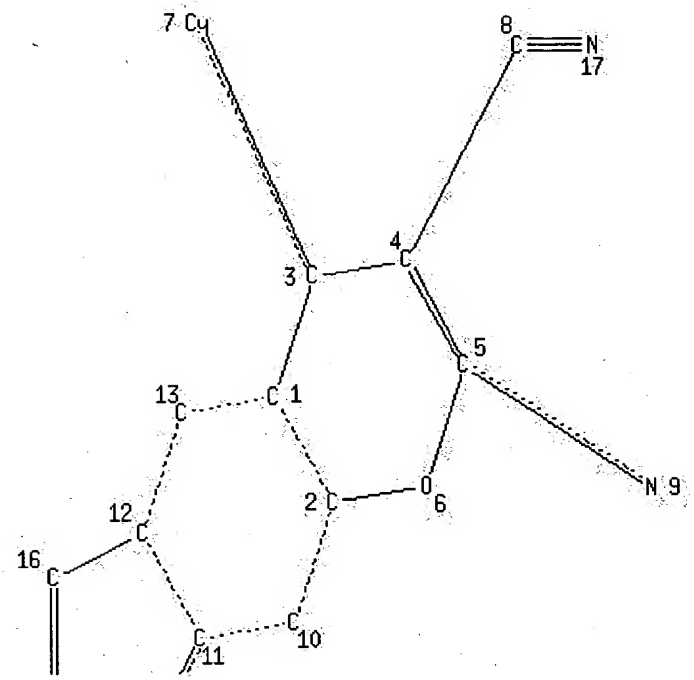
=> 1
1 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> **d l1**
L1 HAS NO ANSWERS
L1 STR

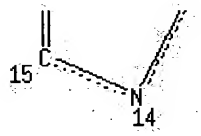


NODE ATTRIBUTES:
NSPEC IS R AT 1
NSPEC IS R AT 2
NSPEC IS R AT 3
NSPEC IS R AT 4
NSPEC IS R AT 5
NSPEC IS R AT 6
NSPEC IS R AT 7
NSPEC IS R AT 8
NSPEC IS R AT 9
NSPEC IS R AT 10
NSPEC IS R AT 11

```
NSPEC   IS R      AT  12
NSPEC   IS R      AT  13
NSPEC   IS C      AT  14
NSPEC   IS C      AT  15
NSPEC   IS RC     AT  16
NSPEC   IS C      AT  17
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT  15 16 17
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  17

STEREO ATTRIBUTES: NONE


=> s l1
SAMPLE SEARCH INITIATED 15:26:27 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     22 TO ITERATE

100.0% PROCESSED      22 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          159 TO      721
PROJECTED ANSWERS:               0 TO        0

L2             0 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 15:26:31 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    448 TO ITERATE

100.0% PROCESSED     448 ITERATIONS                               0 ANSWERS
SEARCH TIME: 00.00.01

L3             0 SEA SSS FUL L1

=>
L4       STRUCTURE UPLOADED

=> d 14
L4 HAS NO ANSWERS
L4               STR
```



Page 1-A



Page 2-A

NODE ATTRIBUTES:

NSPEC	IS R	AT	1
NSPEC	IS R	AT	2
NSPEC	IS R	AT	3
NSPEC	IS R	AT	4
NSPEC	IS R	AT	5
NSPEC	IS R	AT	6
NSPEC	IS C	AT	7
NSPEC	IS C	AT	8
NSPEC	IS RC	AT	9
NSPEC	IS R	AT	10
NSPEC	IS R	AT	11
NSPEC	IS R	AT	12
NSPEC	IS R	AT	13
NSPEC	IS R	AT	14
NSPEC	IS R	AT	15
NSPEC	IS R	AT	16
NSPEC	IS C	AT	17

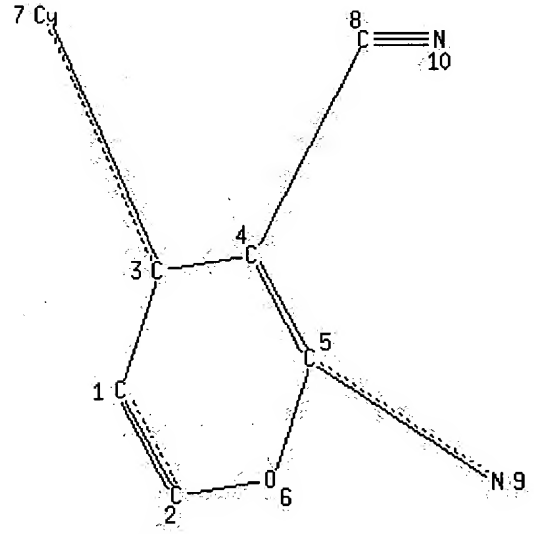
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 8 9 17
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE

=> s 14

```
SAMPLE SEARCH INITIATED 15:27:48 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      23 TO ITERATE

100.0% PROCESSED      23 ITERATIONS                                  0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          173 TO      747
PROJECTED ANSWERS:               0 TO        0

L5             0 SEA SSS SAM L4

=> s l4 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 15:27:51 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     410 TO ITERATE

100.0% PROCESSED     410 ITERATIONS                                  0 ANSWERS
SEARCH TIME: 00.00.01

L6             0 SEA SSS FUL L4

=>
L7       STRUCTURE UPLOADED

=>  l7
L7 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d l7
L7 HAS NO ANSWERS
L7                STR
```




```
NODE ATTRIBUTES:
NSPEC    IS R       AT   1
NSPEC    IS R       AT   2
NSPEC    IS R       AT   3
NSPEC    IS R       AT   4
NSPEC    IS R       AT   5
```

```
NSPEC   IS R      AT   6
NSPEC   IS C      AT   7
NSPEC   IS C      AT   8
NSPEC   IS RC     AT   9
NSPEC   IS C      AT  10
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT   8  9 10
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  10

STEREO ATTRIBUTES: NONE


=> s l7
SAMPLE SEARCH INITIATED 15:28:43 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    778 TO ITERATE

100.0% PROCESSED     778 ITERATIONS                          50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       13887 TO    17233
PROJECTED ANSWERS:           7468 TO     9972

L8            50 SEA SSS SAM L7

=> s l7 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 15:28:48 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  15296 TO ITERATE

100.0% PROCESSED   15296 ITERATIONS                       8733 ANSWERS
SEARCH TIME: 00.00.01

L9          8733 SEA SSS FUL L7

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              468.36     468.57

FILE 'HCAPLUS' ENTERED AT 15:28:51 ON 30 APR 2004
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
```

FILE COVERS 1907 - 30 Apr 2004 VOL 140 ISS 19
FILE LAST UPDATED: 29 Apr 2004 (20040429/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l9/thu
          410 L9
       589364 THU/RL
L10        21 L9/THU
              (L9 (L) THU/RL)

=> s l10 and drewe, j?/au
          164 DREWE, J?/AU
L11         1 L10 AND DREWE, J?/AU

=> d l11, ibib abs fhitstr, 1
```

L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

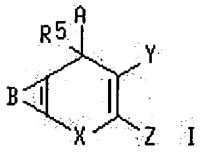
ACCESSION NUMBER: 2001:359984 HCAPLUS
DOCUMENT NUMBER: 134:353254
TITLE: Substituted 4H-chromene and analogs as activators of caspases and inducers of apoptosis and the use thereof
INVENTOR(S): **Drewe, John A.**; Cai, Sui Xiong; Wang, Yan
PATENT ASSIGNEE(S): Cytovia, Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034591	A2	20010517	WO 2000-US30374	20001103
WO 2001034591	A3	20010920		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1230232	A2	20020814	EP 2000-976912	20001103
EP 1230232	B1	20040225		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003513967	T2	20030415	JP 2001-536538	20001103
AT 260269	E	20040315	AT 2000-976912	20001103

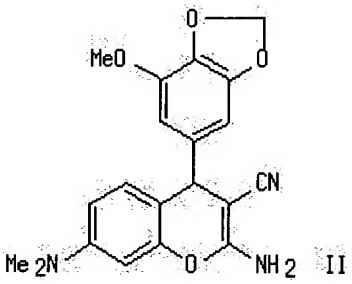
PRIORITY APPLN. INFO.:
US 1999-163584P P 19991105
US 2000-185211P P 20000224
WO 2000-US30374 W 20001103

ND
US 60185211 = Provisional Appln. 60185211 Exp.
US 6165584 60/163584 Expired

OTHER SOURCE(S): MARPAT 134:353254
GI



I



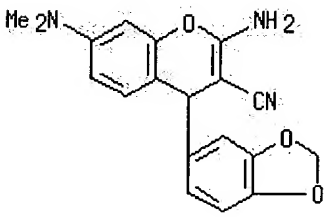
II

AB Title compds. (I) [wherein X = O or S; Y = CN, COR7, CO2R7, or CONRxRy; R7, Rx, and Ry = independently H, (halo)alkyl, (hetero)aryl, fused aryl, carbocyclic, heterocyclic, alkenyl, alkynyl, (hetero)arylalkyl, (hetero)arylalkenyl, (hetero)arylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, or aminoalkyl; or Rx and Ry taken together with the N to which they are attached form a heterocycle; Z = NR8R9, NHCOR8, N(COR8)2, N(COR8)(COR9), N:CHOR8, or N:CHR8; R8 and R9 = independently H, alkyl, or aryl; or R8 and R9 taken together with the group to which they are attached form a heterocycle; R5 = H or alkyl; A = (un)substituted (hetero)aryl, carbocyclic, heterocyclic, or arylalkyl; B = (un)substituted (hetero)arom. ring] were prepd. as activators of caspases and inducers of apoptosis. For example, piperidine was added to a mixt. of 3-dimethylaminophenol, 5-methoxypiperonal, and malonitrile in EtOH to give II (74%). In assays against the human breast cancer cell lines T-47D and ZR-75-1, II showed potent caspase activity (detd. as the ratios of net relative fluorescence units for test compds. compared to control samples of 5.5 and 6.3, resp.) and potency (EC50 = 87 nM and 38 nM, resp.). II also inhibited cell proliferation with GI50 values of 3 nM and 500 nM against T-47D and ZR-75-1, resp. Thus, I may be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs.

IT **339061-54-0P**, 2-Amino-3-cyano-7-dimethylamino-4-(3,4-methylenedioxyphenyl)-4H-chromene
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of substituted 4H-chromene and analogs as activators of caspases and inducers of apoptosis)

RN 339061-54-0 HCAPLUS

CN 4H-1-Benzopyran-3-carbonitrile, 2-amino-4-(1,3-benzodioxol-5-yl)-7-(dimethylamino)- (9CI) (CA INDEX NAME)



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L13  ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

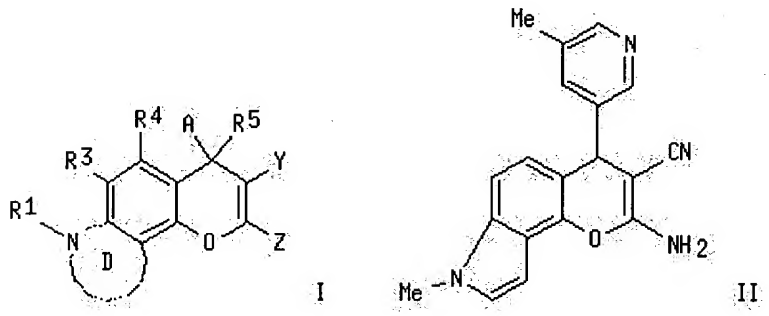
ACCESSION NUMBER: 2003:931479 HCAPLUS
DOCUMENT NUMBER: 140:5049
TITLE: Preparation of substituted 4-aryl-4H-pyrrolo[2,3-h]chromenes and analogs as activators of caspases and inducers of apoptosis and their uses against cancer and other disorders
INVENTOR(S): **Cai, Sui Xiong**; Jiang, Songchun; Kemnitzer, William E.; Zhang, Hong; Attardo, Giorgio; Denis, Real
PATENT ASSIGNEE(S): Cytovia, Inc., USA; Shire Biochem, Inc.
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097806	A2	20031127	WO 2003-US15427	20030516

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-378079P P 20020516
OTHER SOURCE(S): MARPAT 140:5049
GI

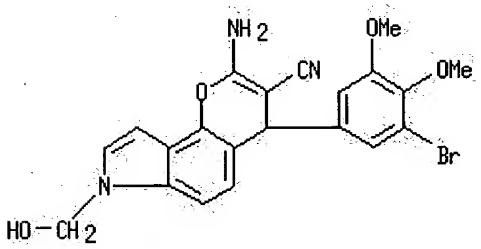


AB The present invention is directed to substituted 4-aryl-4H-pyrrolo[2,3-h]chromenes and analogs thereof (shown as I; variables defined below; e.g. II). The present invention also relates to the discovery that compds. I are activators of caspases and inducers of apoptosis. Therefore, I can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs. The ability to activate the caspase cascade and induce apoptosis in human breast cancer cell lines T-47D and ZR-75-1 was measured for ~50 examples of I, e.g. EC50 (nM) = 2.3 and 1.6, resp., for II. Although the methods of prepn. are not claimed, ~50 example prepns. are included. For I: R1 = alkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, haloalkyl, alkoxyalkyl, aminoalkyl and oxiranylalkyl; R3 and R4 = H, halo, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, C1-10 alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino, cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, methylenedioxy, carbonylamido or alkylthio; R5 is H or C1-10 alkyl. A is (un)substituted and is aryl, heteroaryl, satd. carbocyclic, partially satd. carbocyclic, satd. heterocyclic, partially satd. heterocyclic or arylalkyl; D is (un)substituted and is a heteroarom., partially satd. (un)satd. heterocyclic fused ring, wherein said fused ring has 5 or 6 ring atoms, wherein one or two of said ring atoms are N atoms and the others of said ring atoms are C atoms. Y is CN, COR19, CO2R19 or CONR20R21, wherein R19, R20 and R21 = H, C1-10-alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or R20 and R21 are taken together with the N to form a heterocycle; and Z is NR22R23, NHCOR22N(COR23)2, N(COR22)(COR23), N:CHOR19 or N:CHR19 wherein R22 and R23 = H, C1-4 alkyl or aryl, or R22 and R23 are combined together with the group attached to them to form a heterocycle.

IT **627501-36-4P**, 2-Amino-4-(3-bromo-4,5-dimethoxyphenyl)-3-cyano-7-hydroxymethyl-4H-pyrrolo[2,3-h]chromene
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; prepn. of substituted 4-aryl-4H-pyrrolo[2,3-h]chromenes and analogs as activators of caspases and inducers of apoptosis and their uses against cancer and other disorders)

RN 627501-36-4 HCAPLUS

CN Pyrano[2,3-e]indole-3-carbonitrile, 2-amino-4-(3-bromo-4,5-dimethoxyphenyl)-4,7-dihydro-7-(hydroxymethyl)- (9CI) (CA INDEX NAME)



L13 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:888735 HCAPLUS
DOCUMENT NUMBER: 137:369971
TITLE: Preparation of substituted 4H-chromenes and analogs as activators of caspases and inducers of apoptosis and their uses against cancer and other disorders
INVENTOR(S): **Cai, Sui Xiong**; Zhang, Hong; Jiang, Songchun; Storer, Richard
PATENT ASSIGNEE(S): Cytovia, Inc., USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092594	A1	20021121	WO 2002-US15399	20020516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003065018	A1	20030403	US 2002-146138	20020516
EP 1392683	A1	20040303	EP 2002-741704	20020516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2001-290997P P 20010516
WO 2002-US15399 W 20020516

OTHER SOURCE(S): MARPAT 137:369971
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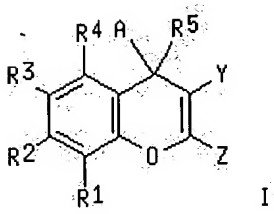


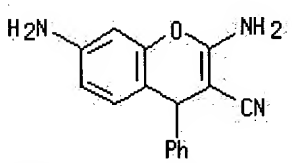
I

AB The present invention is directed to substituted 4H-chromenes and analogs thereof (shown as I; e.g. 2-amino-3-cyano-7-hydroxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene). It also relates to the discovery that I are activators of caspases and inducers of apoptosis and, therefore, can be used to induce cell death in a variety of clin. conditions in which controlled growth and spread of abnormal cells occurs. In I: R1-R4 = H, halo, haloalkyl, aryl, fused aryl, carbocyclic, heterocyclic, heteroaryl, C1-10 alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino, cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, methylenedioxy, carbonylamido or alkylthio; or R1 and R2, or R2 and R3, or R3 and R4, taken together with the atoms to which they are attached form an aryl, heteroaryl, partially satd. carbocyclic or partially satd. heterocyclic group, wherein said group is optionally substituted. R5 is H or C1-10 alkyl; A is optionally substituted and is aryl, heteroaryl, satd. carbocyclic, partially satd. carbocyclic, satd. heterocyclic, partially satd. heterocyclic or arylalkyl; Y is CN, COR7, CO2R7 or CONRxRy, wherein R7, Rx and Ry = H, C1-10 alkyl, haloalkyl, aryl, fused aryl, carbocyclic, heterocyclic, heteroaryl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or Rx and Ry are taken together with the N to which they are attached to form a heterocycle; and Z is NR8R9, NHCOR8, N(COR9)2, N(COR8)(COR9), N:CHOR8 or N:CHR8, wherein R8 and R9 = H, C1-4 alkyl or aryl, or R8 and R9 are combined together with the group attached to them to form a heterocycle. The EC50 values for >80 I against T-47D and ZR-75-1 human breast cancer cell lines are tabulated, e.g. 30 and 25 nM, resp., for 2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-indolo[7,6-b]pyran. Although the methods of prepn. are not claimed, 81 example prepns. are included.

IT **111861-39-3P**, 2,7-Diamino-3-cyano-4-phenyl-4H-chromene
RL: PAC (Pharmacological activity); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; prepn. of substituted 4H-chromenes and analogs as activators of caspases and inducers of apoptosis and their uses against cancer and other disorders)

RN 111861-39-3 HCAPLUS

CN 4H-1-Benzopyran-3-carbonitrile, 2,7-diamino-4-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:888554 HCAPLUS
DOCUMENT NUMBER: 137:384751
TITLE: 7,8-Fused 4(H)-chromenes as activators of caspases and inducers of apoptosis
INVENTOR(S): **Cai, Sui Xiong**; Xu, Lifen; Storer, Richard; Attardo, Giorgio
PATENT ASSIGNEE(S): Cytovia, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

6024076
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092083	A1	20021121	WO 2002-US15398	20020516
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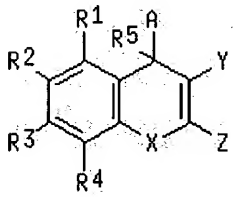
EP 1392294	A1	20040303	EP 2002-731801	20020516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2001-290976P P 20010516
WO 2002-US15398 W 20020516

OTHER SOURCE(S): MARPAT 137:384751
GI



I

AB Title compds. I [X = O, S, (un)substituted NH; Y = CN, (un)substituted CHO, CO2H, CONH2; Z = (un)substituted NH2; R1, R2 = H, halo, haloalkyl, aryl, carbocyclic, heterocyclic, heteroaryl, (un)substituted alkyl, alkenyl, alkynyl, NH2, NO2, CN, OH, SH, acyloxy, N3, alkoxy, CO2H, OCH2O, carbamoyl, alkylthio; R3R4 = atoms required to complete a thiazole, oxazole, 2-iminoimidazole, 2-oxo-2,1,3-thiadiazole, 2-oxothiazole, 2-oxooxazole, 2-thioxooxazole, 2-thioxoimidazole, 2-thioxothazole, imidazoline, oxazoline, thiazoline, triazole, oxazine, 2,3-dioxooxazine, or piperazine ring; R5 = H, alkyl; A = (un)substituted aryl, heteroaryl, carbocyclic, heterocyclic, aralkyl] were prepd. for use as activators of caspases and inducers of apoptosis. Therefore, they can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs. Thus, 2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-7-hydroxy-8-amino-4H-chromene was treated with

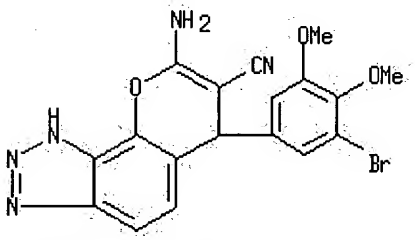
carbonyldiimidazole to give I [X = O, Y = CN, Z = NH2, A = 3,4,5-Br(MeO)2C6H2, R1, R2, R5 = H, R3R4 = OC(O)NH] which had EC50 against T-47D and ZR-75-1 cell lines of 566.6 and 365.6 nM resp.

IT **475659-27-9P**

RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 7,8-fused 4(H)-chromenes as activators of caspases and inducers of apoptosis)

RN 475659-27-9 HCAPLUS

CN Pyrano[2,3-e]benzotriazole-7-carbonitrile, 8-amino-6-(3-bromo-4,5-dimethoxyphenyl)-1,6-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:881133 HCAPLUS
DOCUMENT NUMBER: 134:29313
TITLE: Substituted 5-oxo-5,6,7,8-tetrahydro-4H-1-benzopyrans and benzothiopyrans and their use as potentiators of AMPA
INVENTOR(S): Konkoy, Christopher S.; Fick, David B.; **Cai, Sui Xiong**; Lan, Nancy C.; Keana, John F. W.
PATENT ASSIGNEE(S): Cocensys, Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075123	A1	20001214	WO 2000-US15307	20000605
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EP 1189896	A1	20020327	EP 2000-938095	20000605
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US 6680332	B1	20040120	US 2002-980628	20020520

PRIORITY APPLN. INFO.: US 1999-137501P P 19990604
WO 2000-US15307 W 20000605
OTHER SOURCE(S): MARPAT 134:29313
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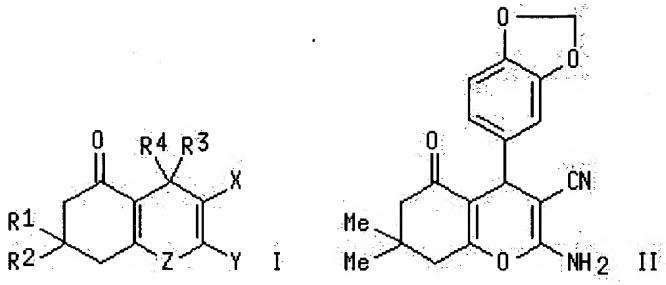
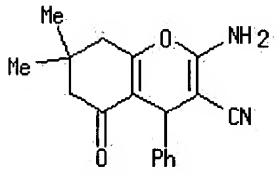


I II

AB Title compds. I [R1, R2 = H, alkyl, alkenyl, alkynyl, arylalkyl, haloalkyl, aryl, heteroaryl, etc.; R3 = H, alkyl; R4 = (un)substituted aryl, heteroaryl, etc.; X = H, NO2, CN, alkyl, aryl, etc.; Y = (un)substituted amino; Z = O, S] were prepd. for treating disorders responsive to the pos. modulation of AMPA receptors. Thus, II was prepd. in 69% yield by reaction of piperonal with malononitrile and 5,5-dimethyl-1,3-cyclohexanedione in the presence of piperidine in 95% EtOH at room temp. The max. potentiation of the AMPA response in Xenopus oocytes by II was 11-fold at 100 μM, half-max. potentiation occurred at 16.6 μM, and a twofold potentiation was elicited at 4 μM.

IT 107752-97-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. as potentiator of AMPA)
RN 107752-97-6 HCAPLUS
CN 4H-1-Benzopyran-3-carbonitrile, 2-amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L9         8733 S L7 FULL

     FILE 'HCAPLUS' ENTERED AT 15:28:51 ON 30 APR 2004
L10          21 S L9/THU
L11           1 S L10 AND DREWE, J?/AU
L12          20 S L10 NOT L11
L13           4 S L12 AND CAI, S?/AU

=> s l12 not l13
L14          16 L12 NOT L13

=> s l14 and wang, y?/au
         39109 WANG, Y?/AU
L15           0 L14 AND WANG, Y?/AU

=> d l14, ibib abs fhitstr, 1-16

L14  ANSWER 1 OF 16  HCAPLUS  COPYRIGHT 2004 ACS on STN
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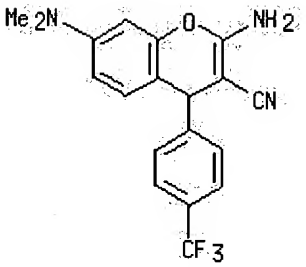
Full Text | Citing References

ACCESSION NUMBER: 2003:146145 HCAPLUS
DOCUMENT NUMBER: 139:79071
TITLE: Identification of Bioactive Molecules by Adipogenesis Profiling of Organic Compounds
AUTHOR(S): Choi, Yongmun; Kawazoe, Yoshinori; Murakami, Koji; Misawa, Hiroyuki; Uesugi, Motonari
CORPORATE SOURCE: The Verna and Marrs McLean Department of Biochemistry and Molecular Biology, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: Journal of Biological Chemistry (2003), 278(9), 7320-7324
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An important step in the postgenomic drug discovery is the construction of high quality chem. libraries that generate bioactive mols. at high rates. Here we report a cell-based approach to composing a focused library of biol. active compds. A collection of bioactive non-cytotoxic chems. was identified from a divergent library through the effects on the insulin-induced adipogenesis of 3T3-L1 cells, one of the most drastic and sensitive morphol. alterations in cultured mammalian cells. The resulting focused library amply contained unique compds. with a broad range of pharmacol. effects, including glucose-uptake enhancement, cytokine inhibition, osteogenesis stimulation, and selective suppression of cancer cells. Adipogenesis profiling of org. compds. generates a focused chem. library for multiple biol. effects that are seemingly unrelated to adipogenesis, just as genetic screens with the morphol. of fly eyes identify oncogenes and neurodegenerative genes.

IT 339063-05-7
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(identification of bioactive mols. by adipogenesis profiling of org. compds.)

RN 339063-05-7 HCAPLUS
CN 4H-1-Benzopyran-3-carbonitrile, 2-amino-7-(dimethylamino)-4-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:123254 HCAPLUS
DOCUMENT NUMBER: 136:161361
TITLE: Method of identifying immunosuppressive agents
INVENTOR(S): Kasibhatla, Shailaja; Green, Douglas R.; Tseng, Ben
PATENT ASSIGNEE(S): Cytovia, Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

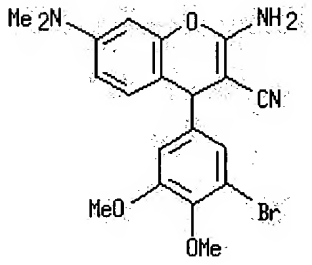
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012545	A2	20020214	WO 2001-US24250	20010802
WO 2002012545	A3	20020801		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001078135	A5	20020218	AU 2001-78135	20010802
US 2002076733	A1	20020620	US 2001-920332	20010802

PRIORITY APPLN. INFO.: US 2000-222897P P 20000803
WO 2001-US24250 W 20010802

AB A method for identifying therapeutically effective immunosuppressive agents by screening such agents for those which induce apoptosis in activated T cells is disclosed. T cells were isolated then activated and treating with various test compds. A caspase substrate is added to detect caspase activation and apoptosis in the cells. Compds. which stimulate caspase activation and apoptosis are also tested against resting T cells to det. those agents which are more effective in activated T cells compared to resting T cells. Compds. with this selectivity are effective in treating immunopathol. disorders such as arthritis, graft rejection, graft vs. host disease, inflammatory bowel syndrome and the like.

IT **339061-63-1**, CV 58151
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(method of identifying immunosuppressive agents by detg. ability to

cause activated T cell apoptosis and caspase activation)
RN 339061-63-1 HCAPLUS
CN 4H-1-Benzopyran-3-carbonitrile, 2-amino-4-(3-bromo-4,5-dimethoxyphenyl)-7-(dimethylamino)- (9CI) (CA INDEX NAME)

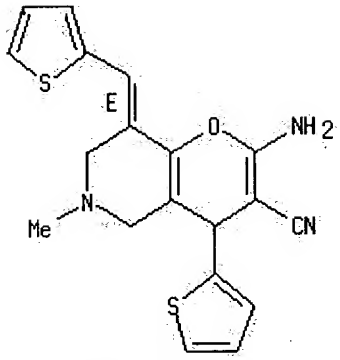


L14 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:38234 HCAPLUS
DOCUMENT NUMBER: 137:149771
TITLE: Antitumor screening of new pyran, pyrazole and pyridine derivatives
AUTHOR(S): Mahran, Mona A.
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Alexandria, Alexandria, 21215, Egypt
SOURCE: Alexandria Journal of Pharmaceutical Sciences (2001), 15(2), 149-151
CODEN: AJPSES; ISSN: 1110-1792
PUBLISHER: University of Alexandria, Faculty of Pharmacy
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Different series of heterocyclic compds. were synthesized and evaluated for antitumor activity. The replacement of N-methylpyridine moiety by a 2,4-dihydroxyphenyl ring was shown to cause a high decrease in antitumor activity. This might be explained on the bases of the drug receptor unfitness of the flat rigid structure of benzene ring compared to the free conformer structures of the heterocyclic system.
IT **288074-13-5**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antitumor screening of new pyran, pyrazole and pyridine derivs.)
RN 288074-13-5 HCAPLUS
CN 4H-Pyrano[3,2-c]pyridine-3-carbonitrile, 2-amino-5,6,7,8-tetrahydro-6-methyl-4-(2-thienyl)-8-(2-thienylmethylene)-, (8E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

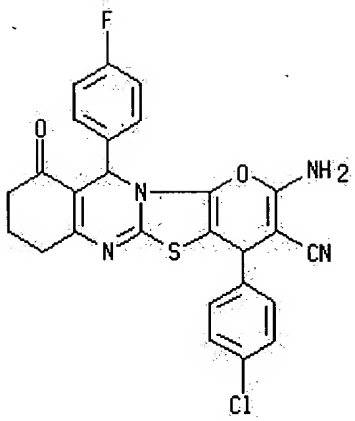
Full Text | Citing References

ACCESSION NUMBER: 2000:530201 HCAPLUS
DOCUMENT NUMBER: 133:237956
TITLE: Synthesis and antifungal activity of novel pyrano[2',3':4,5]thiazolo[2,3-b]quinazolines, pyrido[2',3':4,5]thiazolo[2,3-b]quinazolines and pyrazolo[2',3':4,5]thiazolo[2,3-b]quinazolines
AUTHOR(S): Abdel-Gawad, Soad M.; El-Gaby, Mohamed S. A.; Ghorab, Moustafa M.
CORPORATE SOURCE: Department of Chemistry, Faculty of Science (Girl's), Al-Azhar University, Cairo, Egypt
SOURCE: Farmaco (2000), 55(4), 287-292
CODEN: FRMCE8; ISSN: 0014-827X
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The starting materials thiazolo[2,3-b]quinazolines were obtained in one pot synthesis by treating an octahydroquinazoline deriv. with chloroacetic acid and arom. aldehydes. Pyrano[2',3':4,5]thiazolo[2,3-b]quinazolines and pyrido[2',3':4,5]thiazolo[2,3-b]quinazolinewere prepd. from a thiazolo[2,3-b]quinazoline deriv. Refluxing a thiazolo[2,3-b]quinazoline deriv. with NH2CSNH2/KOH and hydrazines in ethanol furnished the corresponding [1,3]thiazino-[4',5':4,5]thiazolo[2,3-b]quinazoline and pyrazolo[3',4':4,5]thiazolo[2,3-b]quinazolines, resp. Antifungal activity was shown for some of the synthesized compds.

IT **294199-84-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and antifungal activity of thiazoloquinazolines)

RN 294199-84-1 HCAPLUS
CN 4H,8H-Pyrano[2',3':4,5]thiazolo[2,3-b]quinazoline-3-carbonitrile, 2-amino-4-(4-chlorophenyl)-11-(4-fluorophenyl)-7,9,10,11-tetrahydro-10-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:783929 HCAPLUS
DOCUMENT NUMBER: 132:18780
TITLE: Compositions comprising antimicrotubule agents for treating or preventing inflammatory diseases
INVENTOR(S): Hunter, William L.
PATENT ASSIGNEE(S): Angiotech Pharmaceuticals, Inc., Can.
SOURCE: PCT Int. Appl., 340 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

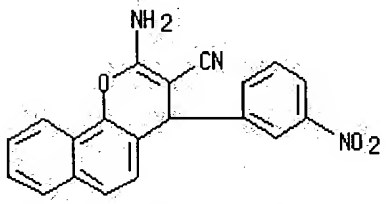
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962510	A2	19991209	WO 1999-CA464	19990601
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6495579	B1	20021217	US 1998-88546	19980601

PRIORITY APPLN. INFO.:		
US 1998-88546	A	19980601
US 1996-32215P	P	19961202
US 1997-63087P	P	19971024
US 1997-980549	A2	19971201

AB Methods and compns. for treating or preventing inflammatory diseases, e.g. psoriasis or multiple sclerosis, are provided, comprising the step of delivering to the site of inflammation an antimicrotubule agent, or analog or deriv. thereof.

IT **149550-36-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antimicrotubule agents for treating or preventing inflammatory diseases)

RN 149550-36-7 HCAPLUS
CN 4H-Naphtho[1,2-b]pyran-3-carbonitrile, 2-amino-4-(3-nitrophenyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:394200 HCAPLUS
DOCUMENT NUMBER: 129:58808
TITLE: Antimicrotubule compositions and methods for treating or preventing inflammatory diseases
INVENTOR(S): Hunter, William L.
PATENT ASSIGNEE(S): Angiotech Pharmaceuticals, Inc., Can.; Hunter, William L.
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9824427	A2	19980611	WO 1997-CA910	19971202
WO 9824427	A3	19981001		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851132	A1	19980629	AU 1998-51132	19971202
AU 735655	B2	20010712		
EP 941089	A2	19990915	EP 1997-945697	19971202
EP 941089	B1	20010516		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1246791	A	20000308	CN 1997-181581	19971202
BR 9713673	A	20001031	BR 1997-13673	19971202
EP 1070502	A2	20010124	EP 2000-123557	19971202
EP 1070502	A3	20011017		
EP 1070502	B1	20030604		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001503785	T2	20010321	JP 1998-524997	19971202
JP 3287852	B2	20020604		
EP 1090637	A2	20010411	EP 2000-123537	19971202
EP 1090637	A3	20010912		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI

EP 1092433	A2	20010418	EP 2000-123534	19971202
EP 1092433	A3	20010912		
EP 1092433	B1	20030806		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

ES 2157601	T3	20010816	ES 1997-945697	19971202
NZ 336094	A	20010831	NZ 1997-336094	19971202
JP 2002226399	A2	20020814	JP 2001-401899	19971202
AT 241977	E	20030615	AT 2000-123557	19971202
AT 246500	E	20030815	AT 2000-123534	19971202
NO 9902641	A	19990730	NO 1999-2641	19990601
MX 9905073	A	20000331	MX 1999-5073	19990601
HK 1022270	A1	20020510	HK 2000-101207	20000228
HK 1033422	A1	20031219	HK 2001-104005	20010612
GR 3036364	T3	20011130	GR 2001-401220	20010810

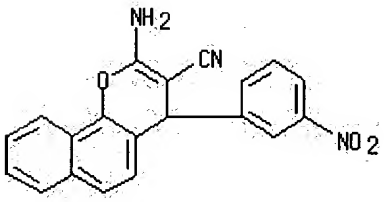
PRIORITY APPLN. INFO.:	US 1996-32215P	P	19961202
	US 1997-63087P	P	19971024
	EP 1997-945697	A3	19971202
	JP 1998-524997	A3	19971202
	WO 1997-CA910	W	19971202

AB The present invention provides methods for treating or preventing inflammatory diseases such as psoriasis or multiple sclerosis, comprising the step of delivering to the site of inflammation an anti-microtubule agent, or analog or deriv. thereof. Antimicrotubule agents include epothilone A or B, discodermolide, deuterium oxide, hexylene glycol, tubercidin, LY290181, aluminum fluoride, ethylene glycol bis(succinimidylsuccinate), glycine Et ester, and paclitaxel.

IT **149550-36-7**, Ly290181
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(antimicrotubule compns. and methods for treating or preventing inflammatory diseases)

RN 149550-36-7 HCAPLUS

CN 4H-Naphtho[1,2-b]pyran-3-carbonitrile, 2-amino-4-(3-nitrophenyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

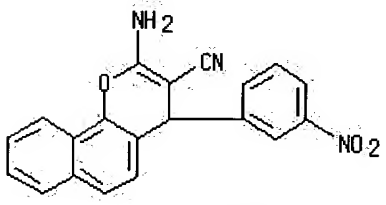
ACCESSION NUMBER:	1997:643500 HCAPLUS
DOCUMENT NUMBER:	127:326456
TITLE:	Inhibition of mitosis and microtubule function through direct tubulin binding by a novel antiproliferative naphthopyran LY290181
AUTHOR(S):	Wood, Dan L.; Panda, Dulal; Wiernicki, Todd R.; Wilson, Leslie; Jordan, Mary Ann; Singh, Jai Pal
CORPORATE SOURCE:	Cardiovascular Res., Lilly Res. Labs., Indianapolis, IN, 46285, USA

SOURCE: Molecular Pharmacology (1997), 52(3), 437-444
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mechanism of action of a novel antiproliferative compd. LY290181 [2-amino-4-(3-pyridyl)-4H-naphtho(1,2-b)pyran-3-carbonitrile] was characterized. LY290181 is a potent inhibitor of cell proliferation, producing 50% inhibition of vascular smooth muscle, endothelial, Chinese hamster ovary, HeLa, and human erythroleukemia cells at concns. of 8-40 nM. Cell cycle anal. showed that LY290181 caused accumulation of smooth muscle cells at the G2/M phase and induced mitotic arrest in Chinese hamster ovary cells and HeLa cells. At low concns. (3-30 nM), LY290181 blocked transition of cells from metaphase to anaphase and disrupted mitotic spindle organization. At high concns. (≤100 nM), LY290181 produced a concn.-dependent loss of cytoplasmic and spindle microtubules. LY290181 inhibited the polymn. of purified bovine brain microtubule protein into microtubules, and it depolymd. preformed microtubules. Using tubulin-1-anilino-8-naphthalene sulfonate complex fluorescence, the authors have shown that LY290181 directly interacted with tubulin in a unique manner. These studies show that LY290181 induces cell growth arrest in prometaphase/metaphase, and tubulin appears to be its mol. target.

IT **149550-36-7**, LY290181
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(inhibition of mitosis and microtubule function through direct tubulin binding by a novel antiproliferative naphthopyran LY290181 in relation to effect on vascular smooth muscle cells in human and lab. animal cells)

RN 149550-36-7 HCAPLUS
CN 4H-Naphtho[1,2-b]pyran-3-carbonitrile, 2-amino-4-(3-nitrophenyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

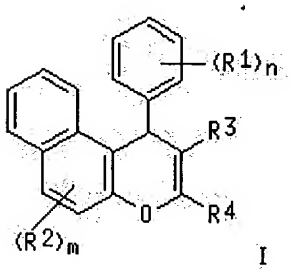
Full Text | Citing References

ACCESSION NUMBER: 1997:224024 HCAPLUS
DOCUMENT NUMBER: 126:212042
TITLE: Phenylnaphthopyrans for treatment of immune system or cell proliferation diseases
INVENTOR(S): Ambler, Samantha Jayne; Heath, William Francis, Jr.; Singh, Jai Pal; Smith, Colin William; Stramm, Lawrence Edward
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: S. African, 28 pp.
CODEN: SFXXAB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ZA 9404689	A	19951229	ZA 1994-4689	19940629

PRIORITY APPLN. INFO.: ZA 1994-4689 19940629
OTHER SOURCE(S): MARPAT 126:212042
GI



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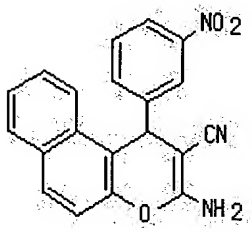
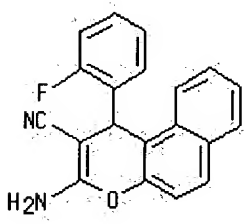


II

AB Phenylnaphthopyrans I [n, m = 0-2; R1, R2 = halo, CF3, OH, NO2, alkoxy, alkylthio, hydroxyalkyl, hydroxyalkoxy, CF3O, (un)esterified CO2H, acyl, carbamoyl; R3 = CN, (un)esterified CO2H; R4 = amino] were prepd. for use in treatment of immune system or cell proliferation diseases, esp. complications of diabetes. Thus, the naphthopyran II was prepd. via condensation of 3-O2NC6H4CHO with CH2(CN)2 in EtOH, followed by cyclization with β-naphthol in the presence of piperidine. II had an ED50 = 0.7 μM in the cellular plasminogen activator and an IC50 = 2.5 μM in the 3H-thymidine DNA incorporation assays.

IT **84186-24-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of phenylnaphthopyrans for treatment of immune system or cell proliferation diseases)
RN 84186-24-3 HCAPLUS
CN 1H-Naphtho[2,1-b]pyran-2-carbonitrile, 3-amino-1-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

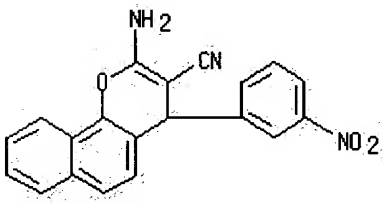
ACCESSION NUMBER: 1996:600138 HCAPLUS
DOCUMENT NUMBER: 125:265467
TITLE: Inhibition of vascular smooth muscle cell proliferation and arterial intimal thickening by a novel antiproliferative naphthopyran
AUTHOR(S): Wiernicki, Todd R.; Bean, James S.; Dell, Colin; Williams, Andrew; Wood, Dan; Kauffman, Raymond F.;

Singh, Jai Pal
CORPORATE SOURCE: Cardiovascular Res., Lilly Res. Lab., Indianapolis, IN, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1996), 278(3), 1452-1459
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Smooth muscle cell proliferation plays an important role in neointimal thickening after vascular injury and may contribute to restenosis after angioplasty. Development of suitable pharmacol. agents modulating smooth muscle cell proliferation is crit. for further investigation of vascular hyperplasia and its prevention. In the present study, we report a novel series of compds. that inhibit smooth muscle cell proliferation and arterial intimal thickening after balloon angioplasty. LY290181 (2-amino-4-[3-pyridyl]-4H-naphtho[1,2-b]pyran-3-carbonitrile) and LY290293 (2-amino-4-[3-pyridyl]-4H-naphtho[1,2-b]pyran-carbonitrile) produced a dose-dependent inhibition of DNA synthesis and proliferation of vascular smooth muscle cells in culture. Fifty percent inhibition (IC50) of cell proliferation was produced by 20 nM LY290181 or LY290293. Cell growth inhibition was not due to cell death, as demonstrated by the release of intracellular lactate dehydrogenase and by the reversibility of inhibition upon washing. Inhibition of smooth muscle cell proliferation was achieved in cells stimulated by either serum or individual growth factor such as platelet-derived growth factor, fibroblast growth factor or epidermal growth factor. In the rat model of balloon injury to carotid artery, LY290181 and LY290293 produced 61% and 48% inhibition of intimal thickening (70%) by LY290293 was also demonstrated when the compd. was administered s.c. at 10 mg/kg/day. These studies demonstrate that naphthopyrans LY290181 and LY290293 are potent inhibitors of smooth muscle cell proliferation in vitro and that they produce substantial redn. in arterial intimal thickening in a balloon injury model when administered systemically.

IT **149550-36-7**, LY290181
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibition of vascular smooth muscle cell proliferation and arterial intimal thickening by a novel antiproliferative naphthopyran)

RN 149550-36-7 HCAPLUS
CN 4H-Naphtho[1,2-b]pyran-3-carbonitrile, 2-amino-4-(3-nitrophenyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

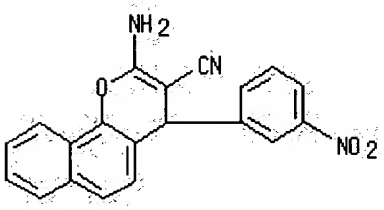
ACCESSION NUMBER: 1996:368630 HCAPLUS
DOCUMENT NUMBER: 125:75783
TITLE: LY290181, an inhibitor of diabetes-induced vascular dysfunction, blocks protein kinase C-stimulated

	transcriptional activation through inhibition of transcription factor binding to a phorbol response element
AUTHOR(S):	Birch, Kimberly A.; Heath, William F.; Hermeling, Ronald N.; Johnston, Cecile M.; Stramm, Larry; Dell, Colin; Smith, Colin; Williamson, Joseph R.; Reifel-Miller, Anne
CORPORATE SOURCE:	Endocrinology Research, Eli-Lilly and Company, Indianapolis, IN, 46285-0424, USA
SOURCE:	Diabetes (1996), 45(5), 642-650 CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER:	American Diabetes Association, Inc.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Previous studies have shown that high glucose levels and diabetes induce an elevation in protein kinase C (PKC) activity in vascular cells and tissues susceptible to diabetic complications. In addn., PKC activation has been shown to modulate vascular cell growth, permeability, and gene expression, processes thought to be involved in the development of vascular complications. Using two in vivo model systems, we have identified a novel inhibitor of diabetic vascular dysfunction, LY290181. LY290181 prevented glucose-induced increases in blood flow and permeability in rat granulation tissue and corresponding vascular changes in the retina, sciatic nerve, and aorta of diabetic rats. Tested for its ability to inhibit PKC-regulated processes, LY290181 inhibited phorbol ester-stimulated plasminogen activator activity in a dose-dependent manner in bovine retinal endothelial cells and in human dermal fibroblasts. In addn., LY290181 inhibited phorbol ester-stimulated activation of the porcine urokinase plasminogen activator (uPA) promoter (-4600/+398) linked to the chloramphenicol acetyltransferase (CAT) reporter gene (p4660CAT). More detailed anal. of the uPA promoter revealed that LY290181 inhibited phorbol ester-stimulated activation of the uPA phorbol response element (-2458/-2349) located upstream of the thymidine kinase promoter (puPATKCAT). LY290181 appears to inhibit uPA promoter activation by blocking phorbol ester-stimulated binding of nuclear proteins to the uPA PEA3/12-O-tetradecanoylphorbol 13-acetate responsive element (TRE). These results suggest that LY290181 may inhibit diabetes-induced vascular dysfunction by inhibiting transcription factor binding to specific PKC-regulated genes involved in vascular function.

IT **149550-36-7**, LY 290181
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(LY290181, an inhibitor of diabetes-induced vascular dysfunction, blocks protein kinase C-stimulated transcriptional activation through inhibition of transcription factor binding to a phorbol response element)

RN 149550-36-7 HCAPLUS
CN 4H-Naphtho[1,2-b]pyran-3-carbonitrile, 2-amino-4-(3-nitrophenyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

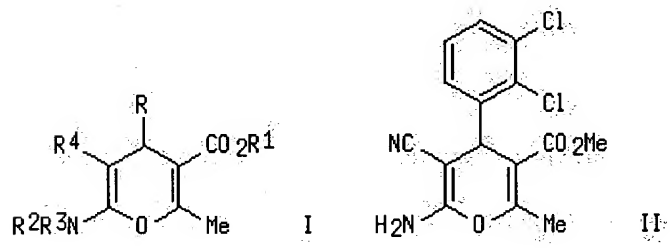
Full Text | Citing References

ACCESSION NUMBER: 1996:271493 HCAPLUS
DOCUMENT NUMBER: 124:316988
TITLE: Preparation of 6-amino-4-aryl-5-cyano-4H-pyran-3-carboxylates as CNS potassium channel modulators
INVENTOR(S): Urbahns, Klaus; Heine, Hans-Georg; Junge, Bodo; Schohe-Loop, Rudolf; Sommermeyer, Henning; Glaser, Thomas; Wittka, Reilinde; de Vry, Jean
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 7 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4429786	A1	19960229	DE 1994-4429786	19940823
TW 429147	B	20010411	TW 1995-84107281	19950714
CA 2198129	AA	19960229	CA 1995-2198129	19950810
WO 9606091	A1	19960229	WO 1995-EP3168	19950810
W: AU, BY, CA, CN, CZ, EE, FI, HU, JP, KR, LT, LV, MX, NO, NZ, PL, RU, SI, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9533439	A1	19960314	AU 1995-33439	19950810
EP 777663	A1	19970611	EP 1995-929833	19950810
EP 777663	B1	19990526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10504312	T2	19980428	JP 1995-507746	19950810
AT 180478	E	19990615	AT 1995-929833	19950810
ES 2131850	T3	19990801	ES 1995-929833	19950810
IL 115004	A1	20001031	IL 1995-115004	19950821
ZA 9507015	A	19960409	ZA 1995-7015	19950822
US 5874462	A	19990223	US 1997-793068	19970214

PRIORITY APPLN. INFO.: DE 1994-4429786 A 19940823
WO 1995-EP3168 W 19950810

OTHER SOURCE(S): MARPAT 124:316988
GI



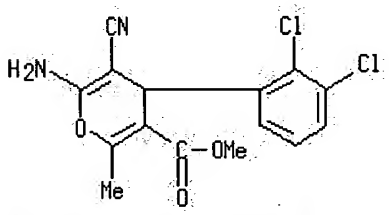
AB Title compds. [I; R = (un)substituted aryl, -pyridyl; R1 = H, alkyl; R2,R3 = H, alkyl, acyl; R4 = cyano, NO2, alkoxycarbonyl] were prepd. as CNS potassium channel modulators (no data). Thus, 2,3-Cl2C6H3CH:C(COMe)CO2Me was cyclocondensed with CH2(CN)2 to give title compd. II.

IT 176106-05-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 6-amino-4-aryl-5-cyano-4H-pyran-3-carboxylates as CNS potassium channel modulators)

RN 176106-05-1 HCAPLUS

CN 4H-Pyran-3-carboxylic acid, 6-amino-5-cyano-4-(2,3-dichlorophenyl)-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

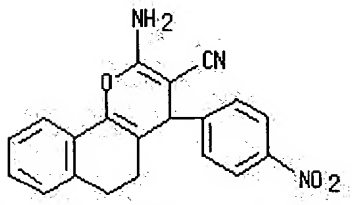
Full Text | Citing References

ACCESSION NUMBER: 1995:644408 HCAPLUS
DOCUMENT NUMBER: 123:131988
TITLE: Identification of a novel chemical series that blocks interleukin-1-stimulated metalloprotease activity in chondrocytes
AUTHOR(S): Chandrasekhar, Srinivasan; Harvey, Anita K.; Dell, Colin P.; Ambler, Samantha J.; Smith, Colin W.
CORPORATE SOURCE: Skeletal Diseases Group, Lilly Res. Laboratories Corp. Center, Indianapolis, IN, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1995), 273(3), 1519-28
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cartilage destruction is one of the essential features of osteoarthritis and other degenerative disease conditions of articular disease, and it may be caused by metalloproteases induced by cytokines such as interleukin-1. To search for novel chem. entities that will block the prodn. of metalloproteases, we have utilized an in vitro system in which macrophage-conditioned medium (a source of interleukin-1) was used to stimulate rabbit articular chondrocytes in culture. Upon treatment with macrophage-conditioned medium or recombinant interleukin-1, chondrocytes synthesize and secrete collagenase, stromelysin and other proteases into the surrounding medium and fail to organize an appropriate extracellular matrix. Using this in vitro system, we have detd. that a series of naphthopyran derivs. were able to block the prodn. of neutral metalloproteases. Structural modifications of the lead compd. have revealed specific requirements for activity. This class of compds. represents one of very few that are known to block the synthesis, rather than the activity, of matrix-degrading metalloproteases and thus may be beneficial in preventing the cartilage destruction assocd. with several degenerative diseases of the articular joint.

IT **70382-91-1**, LY 270211
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(naphthopyran derivs. block interleukin 1-stimulated metalloprotease activity in chondrocyte and role in therapy of osteoarthritis)

RN 70382-91-1 HCAPLUS
CN 4H-Naphtho[1,2-b]pyran-3-carbonitrile, 2-amino-5,6-dihydro-4-(4-nitrophenyl)- (9CI) (CA INDEX NAME)



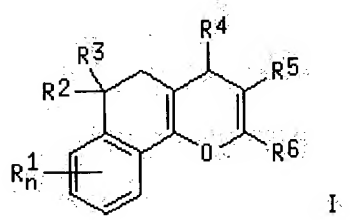
L14 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1995:444299 HCAPLUS
DOCUMENT NUMBER: 122:213932
TITLE: Preparation of 2-aminodihydronaphtho[1,2-b]pyran-3-carbonitriles and analogs as immunomodulators and antiproliferative agents
INVENTOR(S): Dell, Colin Peter; Owton, William Martin
PATENT ASSIGNEE(S): Lilly Industries Ltd., UK
SOURCE: Brit. UK Pat. Appl., 20 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2279951	A1	19950118	GB 1993-14778	19930716
GB 2279951	B2	19970716		

PRIORITY APPLN. INFO.: GB 1993-14778 19930716
OTHER SOURCE(S): MARPAT 122:213932
GI

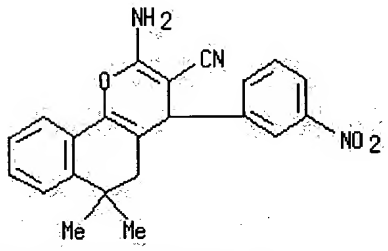


I

AB Title compds. [I; R1 = halo, OH, alkyl, alkoxy, CO2H, etc.; R2,R3 = alkyl; R4 = (un)substituted (hetero)aryl; R5 = cyano, CO2H, alkoxycarbonyl, CONH2, etc.; R6 = (bis)(alkanoyl)amino, N:CHOMe, etc.; n = 0-2] were prepd. Thus, 4,4-dimethyl-1-tetralone was condensed with 3-(O2N)C6H4CHO and the benzylidene aldol product cyclocondensed with CH2(CN)2 to give I [R2 = R3 = Me, R4 = 3-(O2N)C6H4, R5 = cyano, R6 = NH2]. I had IC50 of <20μM against natural proliferation of 3T3 fibroblasts.

IT **161802-45-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-aminodihydronaphtho[1,2-b]pyran-3-carbonitriles and analogs as immunomodulators and antiproliferative agents)

RN 161802-45-5 HCAPLUS
CN 4H-Naphtho[1,2-b]pyran-3-carbonitrile, 2-amino-5,6-dihydro-6,6-dimethyl-4-(3-nitrophenyl)- (9CI) (CA INDEX NAME)



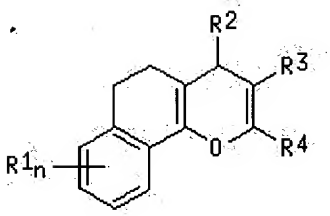
L14 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

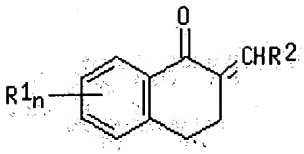
ACCESSION NUMBER: 1995:331667 HCAPLUS
DOCUMENT NUMBER: 122:178407
TITLE: Preparation of naphthopyrans for treatment of diabetic complications
INVENTOR(S): Brunavs, Michael; Dell, Colin P.; Gallagher, Peter T.; Owton, William M.; Smith, Colin W.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: U.S., 9 pp. Cont.-in-part of U.S. Ser. No. 14,016.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5378717	A	19950103	US 1993-34059	19930322
US 5378699	A	19950103	US 1993-14016	19930205
US 5663375	A	19970902	US 1994-293786	19940822
US 5622987	A	19970422	US 1995-461342	19950605
PRIORITY APPLN. INFO.:			US 1993-14016	19930205
			GB 1992-3497	19920219
			US 1994-293786	19940822

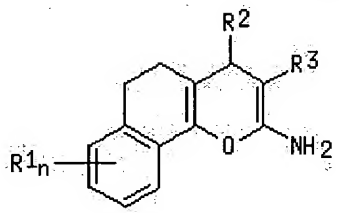
OTHER SOURCE(S): MARPAT 122:178407
GI



I



II



III

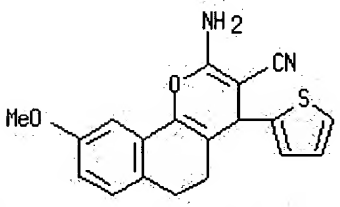
AB Vascular dysfunction in diabetes can be treated with (I), R1 = C1-C4 alkoxy, OH, or COOH; R2 = Ph, naphthyl or heteroaryl; R3 = nitrile; and R4 = NR11R12, NR11COR12, or N:CHOCH2R11 where R11 and R12 are H or C1-4 alkyl. I were prepd. by reacting II with malononitrile or by converting III to I.

IT **151886-11-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of naphthopyrans for treatment of diabetic complications)

RN 151886-11-2 HCAPLUS

CN 4H-Naphtho[1,2-b]pyran-3-carbonitrile, 2-amino-5,6-dihydro-9-methoxy-4-(2-thienyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1995:248558 HCAPLUS
DOCUMENT NUMBER: 122:31327
TITLE: Preparation of 4-phenyl-4H- naphtho(2,1-b)pyran derivatives and their pharmaceutical use.
INVENTOR(S): Ambler, Samantha Jayne; Heath, William Francis, Jr.; Singh, Jai Pal; Smith, Colin William; Stramm, Lawrence Edward
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

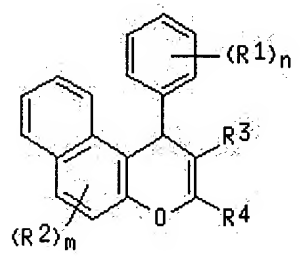
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 619314	A1	19941012	EP 1994-302395	19940405	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
JP 06321929	A2	19941122	JP 1994-69286	19940407	
CA 2120861	AA	19941010	CA 1994-2120861	19940408	
US 5514706	A	19960507	US 1994-342993	19941121	
US 5624953	A	19970429	US 1996-594613	19960202	

PRIORITY APPLN. INFO.: US 1993-45396 19930409
US 1994-342993 19941121

OTHER SOURCE(S): MARPAT 122:31327

GI



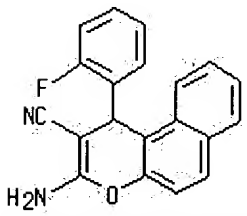
I

AB Title compds. I (R1, R2 = halo, F3C, C1-4 alkoxy, HO, O2N, C1-4 alkyl, F3CO, HO2C (substituted) H2NCO, etc.; R3 = NC, HO2C, R11O2C wherein R11 = ester; R4 = (substituted)amino, (substituted) HCONH, etc.; m, n = 0-2) or a salt thereof, useful for treatment of restenosis, immune disease, and diabetic complications, are prepd. 3-Nitrobenzaldehyde and malononitrile in EtOH were refluxed to give the 3-nitrobenzylidenemalononitrile, to which was added 2-naphthol followed by piperidine to give I (R1n = 3-O2N, R2m = 0, R3 - NC, R4 = H2N). A similar prepd. compd I (R1n = 3-F3C, R2m = 0, R3 = NC, R4 = H2N) (II). The ED50 of II of alterations in cellular plasminogen activator activity in cell lysates was 0.05 μM and IC50 in 3H-thymidine incorporation model for treatment of restenosis was 0.5 μM. Capsule and tablet formulations of I are given.

IT **84186-24-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of phenylnaphthopyran derivs. and their pharmaceutical use.)

RN 84186-24-3 HCAPLUS

CN 1H-Naphtho[2,1-b]pyran-2-carbonitrile, 3-amino-1-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

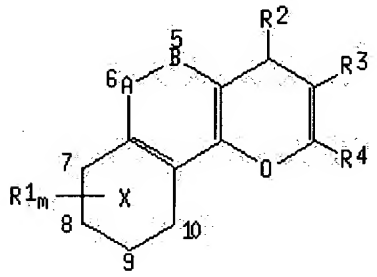
ACCESSION NUMBER: 1995:231221 HCAPLUS
DOCUMENT NUMBER: 122:9869
TITLE: Preparation of naphthopyran and pyranoquinoline immunosuppressants and cell proliferation inhibitors

INVENTOR(S): Williams, Andrew Caerwyn
PATENT ASSIGNEE(S): Lilly Industries Ltd., UK
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 618206	A1	19941005	EP 1994-302040	19940322
EP 618206	B1	19970917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2119530	AA	19940925	CA 1994-2119530	19940321
US 5514699	A	19960507	US 1994-215344	19940321
AT 158291	E	19971015	AT 1994-302040	19940322
ES 2107129	T3	19971116	ES 1994-302040	19940322
JP 07002845	A2	19950106	JP 1994-50918	19940323
US 5571818	A	19961105	US 1995-461343	19950605
US 5574034	A	19961112	US 1995-463838	19950605
US 5576325	A	19961119	US 1995-463530	19950606

PRIORITY APPLN. INFO.: GB 1993-6062 19930324
US 1994-215344 19940321

OTHER SOURCE(S): MARPAT 122:9869
GI

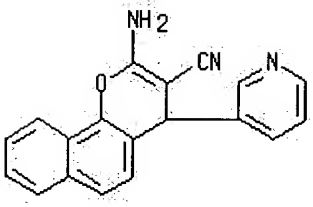


I

AB The title compds. [I; A-B = CH2CH2, CH:CH; R1 = halogen, (un)substituted alkyl, CF3, OH, NO2, N-contg. heterocyclyl, etc.; R2 = (un)substituted Ph, (un)substituted naphthyl, (un)substituted heteroaryl; R3 = CN, (un)substituted carboxy, etc.; R4 = (un)substituted 1-pyrrolyl, (un)substituted 1-imidazolyl, (un)substituted 1-pyrazolyl; X = pyridine or benzene ring; n = 0-2; when X = pyridine then n = 0; when X = benzene ring then n = 0-2 and when A-B = CH2CH2 then R1 may be attached at postions 7-10 but when A-B = CH:CH then R1 may be attached at positions 5-10], useful in the treatment of immune diseases (no data) and diseases where excess cell proliferation (no data) or enzyme release (no data) play a significant role, are prepd. and I-contg. formulations are presented. Thus, 4-(3-nitrophenyl)-2-(1-pyrrolyl)-4H-naphtho[1,2-b]pyran-3-carbonitrile, m.p. 197.5-198.5°, was prepd.

IT **149550-46-9P**
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of naphthopyran and pyranoquinoline immunosuppressants and cell proliferation inhibitors)

RN 149550-46-9 HCAPLUS
CN 4H-Naphtho[1,2-b]pyran-3-carbonitrile, 2-amino-4-(3-pyridinyl)- (9CI) (CA INDEX NAME)

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    111.68     580.25

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -14.55     -14.55

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FILE COVERS 1907-1966
FILE LAST UPDATED:  01 May 1997 (19970501/UP)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.  Title keywords, authors, patent
  assignees, and patent information, e.g., patent numbers, are
  now searchable from 1907-1966.  TIFF images of CA abstracts
  printed between 1907-1966 are available in the PAGE
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  This file supports REG1stRY for direct browsing and searching of
  all substance data from the REGISTRY file.  Enter HELP FIRST for
  more information.

=> d his

     (FILE 'HOME' ENTERED AT 15:24:06 ON 30 APR 2004)

     FILE 'REGISTRY' ENTERED AT 15:24:11 ON 30 APR 2004
L1                STRUCTURE UPLOADED
L2            0 S L1
L3            0 S L1 FULL
L4                STRUCTURE UPLOADED
L5            0 S L4
L6            0 S L4 FULL
L7                STRUCTURE UPLOADED
L8           50 S L7
L9         8733 S L7 FULL

     FILE 'HCAPLUS' ENTERED AT 15:28:51 ON 30 APR 2004
L10          21 S L9/THU
L11           1 S L10 AND DREWE, J?/AU
L12          20 S L10 NOT L11
L13           4 S L12 AND CAI, S?/AU
L14          16 S L12 NOT L13
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L15             0 S L14 AND WANG, Y?/AU

     FILE 'CAOLD' ENTERED AT 15:32:05 ON 30 APR 2004

=> s l9
L16             2 L9

=> d l16, all, 1-2

L16  ANSWER 1 OF 2  CAOLD  COPYRIGHT 2004 ACS on STN
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Full Text

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AN   CA59:13952c  CAOLD
TI   warfarin intermediates
AU   Wiener, Charles; Schroeder, C. H.; Link, K. P.
PA   Wisconsin Alumni Research Foundation
DT   Patent
     PATENT NO.     KIND          DATE
     ------------   -----------   ----
PI   US 3097213                   1963
IT   4958-06-9  94305-90-5  94308-10-8  94549-94-7  96767-93-0  98782-68-4

L16  ANSWER 2 OF 2  CAOLD  COPYRIGHT 2004 ACS on STN
AN   CA57:12413f  CAOLD
TI   4-hydroxycoumarins - (XVIII) 3-[α-(acetamidomethyl)benzyl]-4-
     hydroxycoumarin and related products
AU   Wiener, Charles; Schroeder, C. H.; West, B. D.; Link, K. P.
IT   4610-30-4  4958-06-9  17173-83-0  38063-51-3  92962-58-8  92962-59-9
     94257-20-2  94257-22-4  94305-90-5  94308-10-8  94549-94-7  96767-93-0
     97442-11-0


=> fil reg; d acc 96767-93-0; fil CAOLD

FILE 'REGISTRY' ENTERED AT 15:32:41 ON 30 APR 2004


ANSWER 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   96767-93-0  REGISTRY
CN   4H,5H-Pyrano[3,2-c][1]benzopyran-3-carbonitrile, 2-amino-5-oxo-4-phenyl-
     (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   4H-Pyran-3-carboxylic acid, 6-amino-5-cyano-2-(o-hydroxyphenyl)-4-phenyl-,
     δ-lactone (7CI)
FS   3D CONCORD
MF   C19 H12 N2 O3
LC   STN Files:   BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, TOXCENTER
         (*File contains numerically searchable property data)
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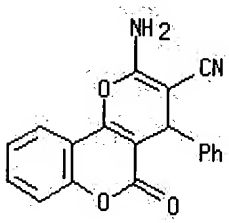


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
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             9 REFERENCES IN FILE CA (1907 TO DATE)
             9 REFERENCES IN FILE CAPLUS (1907 TO DATE)
             2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)


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